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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,417	03/12/2004	Paul A. Krieg	20825-0004	6904

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/799,417	KRIEG, PAUL A.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-59 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-59 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-59 are all the pending claims for this application and all the claims subject to restriction/election of species requirement.

Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-30, drawn to a method of inhibiting angiogenesis or tumorigenesis in a biological sample or in a patient comprising combining an inhibitor of apelin and an anti-cancer agent with the sample or administering the combination to the patient, classified in class 424, subclass 130.1.

II. Claims 31-32, drawn to a method of decreasing vascular permeability in a biological sample from a patient comprising combining the sample with an apelin inhibiting agent, classified in class 424, subclass 130.1.

III. Claims 33-50, drawn to a method of promoting angiogenesis in a biological sample comprising combining the sample with an angiogenesis promoting agent comprising apelin activity, classified in class 514, subclass 2.

IV. Claims 51-59, drawn to a method for identifying a modulator of angiogenesis comprising combining apelin and a putative modulator of angiogenesis and administering the composition to an angiogenesis

predictive model to compare vascular branching, classified in class 424, subclass 130.1.

The inventions are distinct and separate for the following reasons:

3. The methods of Groups I-IV differ in the method objectives, method steps and parameters, intended populations and in the reagents used. The method of Group I requires providing a biological sample and combining the sample with an angiogenesis inhibiting amount of an inhibitor for apelin activity and an anti-cancer agent in order to inhibit angiogenesis or tumorigenesis in the sample or in the patient; the method of Group II requires providing a biological sample and combining the sample with a vascular permeability-decreasing amount of an apelin activity inhibitor in order to decrease vascular permeability; the method of Group III requires providing a biological sample and combing the sample and an angiogenesis promoting composition comprising apelin activity in order to promote angiogensis; and the method of Group IV requires an angiogenesis predictive model and combining an angiogenesis promoting composition comprising apelin and a putative angiogenesis modulator for administration to the model, where after administration of the composition the amount of vascular branching is observed in order to identify a modulator of angiogenesis. The examination of all groups would require different searches in the U.S. and foreign patent literature and the scientific literature and would require the consideration of different patentability issues. Thus Inventions of Groups I-IV are separate and distinct in having different method steps, intended populations and different reagents and are patentably distinct.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper. In addition to their distinctness, searching the methods would impose a serious search burden as in the instant case where the searches of the methods is not co-extensive

Election of Species

5. If Group I is elected, the following species are found in the claims. This application contains claims directed to the following patentably distinct species (inhibitor for apelin activity) of the claimed invention:

Specie A) inhibitor affecting apelin

Specie B) inhibitor affecting APJ (apelin receptor)

The species A and B represent distinct and separate inhibitory agents and are non-obvious variants, because each has a unique chemical structure and the functional properties (e.g., pharmacological and pharmaceutical) for each species is unique and unrelated. The target for each inhibitor is structurally and functionally different, one skilled in the art would recognize that the inhibitor for an apelin protein target was not interchangeable with one for the apelin receptor. The species are not obvious variants or overlapping, thus to search the species together would present a search burden due to the extensive databases of non-patent literature and because searching the databases is not co-extensive.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-6 and 21-30 are generic as to species A and B.

6. If any one of Groups I or II is elected, the following species are found in the claims. This application contains claims directed to the following patentably distinct species (disease or condition) of the claimed invention (see claims 27 and 32): stroke, hemangioma, solid tumors, leukemias, lymphomas, myelomas, metastasis, telangiectasia psoriasis scleroderma, pyogenic granuloma, Myocardial angiogenesis, plaque neovascularization, cororany collaterals, ischemic limb angiogenesis, comeal diseases, rubeosis, neovascular glaucoma, diabetic retinopathy, retrolental fibroplasia, arthritis, diabetic neovascularization, macular degeneration, wound healing, peptic ulcer, fractures, keloids, vasculogenesis, hematopoiesis, ovulation, menstruation, placentation, polycystic ovary syndrome, dysfunctional uterine bleeding, endometrial hyperplasia and carcinoma, endometriosis, failed implantation and subnormal foetal growth, myometrial fibroids (uterine leiomyomas) and adenomyosis, ovarian hyperstimulation syndrome, and ovarian carcinoma.

Each of the diseases or conditions is separate and distinct. The different diseases or conditions originate from any number of different cell types. Also, the disorders or conditions being associated with different organs and tissues, are under the influence of different growth factors, hormones, cytokines, etc, and are distinguishable

by whether they are chronic, acute or both. Additionally, numerous studies have shown that receptor density and affinity for different therapeutic biomolecules is highly variable amongst different tissues and organs, in addition to there being differences to the extent to which biomolecules are able to penetrate tissues and organs. This suggests that any method inventions involving administering the apelin activity inhibitor in the realm of a disorder or condition, would require different routes of administration, dosing, formulation, sensitivity of detection, etc., and that one could not predict biodistribution of the inhibitor in a subject much less an outcome of success for treating all disorders or conditions in following the same method steps or using the same conditions. The species are not obvious variants or overlapping, thus to search the species together would present a search burden due to the extensive databases of non-patent literature and because searching the databases is not co-extensive.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-26 and 28-31 are generic as to the species.

7. If Group III is elected, the following species are found in the claims. This application contains claims directed to the following patentably distinct species (apelin activity comprising composition) of the claimed invention:

Specie A) serine protease

Specie B) apelin polypeptide (SEQ ID NOS: 1-5)

Specie C) small molecule agonist

The species represent distinct and separate apelin activity comprising compositions and are non-obvious variants, because each has a unique chemical structure and the functional properties (e.g., pharmacological and pharmaceutical) for each species is unique and unrelated. The species are not obvious variants or overlapping, thus to search the species together would present a search burden due to the extensive databases of non-patent literature and because searching each of the species in the databases is not co-extensive.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 33, 34 and 44-50 are generic as to species A-C.

Election of Nested Species

8. If Group I and the species apelin inhibitor is elected, the following nested species are found in the claims. This application contains claims directed to the following patentably distinct nested species (apelin inhibitor) of the claimed invention:

Specie A) anti-apelin antibody (binding to one polypeptide of SEQ ID NO:1-5)

Specie B) apelin antisense nucleic acid

Specie C) receptor decoy

Specie D) ribozyme

Specie E) sense polynucleotide

Specie F) double standed RNA

Specie G) RNAi

Specie H) aptamer

Specie I) small molecule antagonist

Specie J) serine protease inhibitor

The species represent distinct and separate apelin inhibiting agents and are non-obvious variants, because each has a unique chemical structure and the functional properties (e.g., pharmacological, pharmaceutical, clinical) for each species is unique and unrelated. The species are not obvious variants or overlapping, thus to search the species together would present a search burden due to the extensive databases of non-patent literature and because searching each of the species in the databases is not co-extensive.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-6, 15-17, 19, 21-30 are generic as to species A-J.

9. If Group I and the species apelin receptor (APJ) inhibitor is elected, the following nested species are found in the claims. This application contains claims directed to the following patentably distinct nested species (apelin receptor (APJ) inhibitor) of the claimed invention:

Specie A) anti-apelin receptor (APJ) antibody (binding to polypeptide of SEQ ID NO: 17)

Specie B) apelin receptor (APJ) antisense nucleic acid

Specie C) receptor decoy

Specie D) ribozyme

Specie E) sense polynucleotide

Specie F) double standed RNA

Specie G) RNAi

Specie H) aptamer

Specie I) small molecule antagonist

The species represent distinct and separate apelin receptor inhibiting agents and are non-obvious variants, because each has a unique chemical structure and the functional properties (e.g., pharmacological, pharmaceutical, clinical) for each species is unique and unrelated. The species are not obvious variants or overlapping, thus to search the species together would present a search burden due to the extensive databases of non-patent literature and because searching each of the species in the databases is not co-extensive.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-14, 18, 21-30 are generic as to species A-I.

10. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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SUPERVISORY PATENT EXAMINER